ACR/ARHP Annual Meeting
Washington, DC • 2016

# ACR MEET THE PROFESSOR

## 005 - Pulmonary Manifestations of Rheumatic Disease

November 13, 2016

7:45 AM – 9:15 AM

**Paul F. Dellaripa, MD**

## Meeting Disclaimer

The ACR/ARHP Annual Meeting Planning Committee has independently planned the 2016 ACR/ARHP Annual Meeting. This program is sponsored by the American College of Rheumatology.

The ACR/ARHP makes every effort to collect syllabi from each speaker. Due to the confidentiality of the studies/information being presented, we regret that we are not able to publish all syllabi. To ensure that the latest information is presented, some speakers may update syllabi prior to their presentation. Therefore, syllabi and presentations may differ.

The ACR and ARHP are independent professional organizations that do not endorse specific products of any pharmaceutical concern.

The material presented is not intended to represent the only or the best methods appropriate for the medical situations discussed, but rather are intended to present the opinions of the authors or presenters, which may be helpful to other practitioners.

Attendees participating in this activity do so with full knowledge that they waive any claim they might have against the ACR/ARHP for reliance on any information presented.

## Accreditation Statement

The American College of Rheumatology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The American College of Rheumatology designates this educational activity for a maximum of 1.5 *AMA PRA Category 1 Credit(s)*$^{TM}$. Physicians should only claim credit commensurate with the extent of their participation in the activity.

## Conflict of Interest and Disclosure

As an educational provider accredited by the Accreditation Council for Continuing Medical Education, the American College of Rheumatology must ensure balance, independence, objectivity and scientific rigor in all its educational activities. Therefore, all those in a position to control content (e.g., speakers and moderators) participating in an ACR-sponsored activity are required to disclose to the planning committee and audience any financial or other relationships including, but not limited to:

None: Nothing to disclose

1. Stock, stock options or bond holdings in a for-profit corporation or self-directed pension plan
2. Research grants
3. Employment (full or part-time)
4. Ownership or partnership
5. Consulting fees or other remuneration (payment)
6. Non-remunerative positions of influence such as officer, board member, trustee or public spokesperson
7. Receipt of royalties
8. Speakers' bureau
9. Other

Speakers and abstract authors were required to submit their disclosure online prior to publication. Any individual who refuses to disclose relevant financial relationships is ineligible to serve as a planning committee member,

presenter, or an author of an ACR CME activity, and cannot have control of, or responsibility for, the development, management, presentation or evaluation of the CME activity.

## Copyright Materials Policy

The annual meeting is a private event. Programs presented at the meeting are for the education of attendees and purchasers of recorded presentations as authorized by the American College of Rheumatology. Information displayed or presented at all sessions during the annual meeting is the property of the ACR or the presenter. Information may not be recorded, photographed, copied, photocopied, transferred to electronic format, reproduced or distributed without the written permission of the ACR and the presenter. Any use of the program content, which includes but is not limited to oral presentations, audiovisual materials used by speakers and program handouts, without the written consent of the ACR is prohibited. This policy applies before, during and after the meeting. The ACR will enforce its intellectual property rights and penalize those who infringe upon it.

**Use of American College of Rheumatology's Name**

The names, insignias, logos and acronyms of the ACR, the ARHP and the ACR Research and Education Foundation are proprietary marks. Use of the names in any fashion, by any entity, for any purpose, is prohibited without the written permission of the College.

## Disclosure Policy

It is the policy of the American College of Rheumatology to ensure that its CME activities are independent and free of commercial bias.

To ensure content objectivity and balance, and guarantee that the content presented is in the best interest of its learners and the public, the ACR requires that all individuals in a position to control content disclose all relevant financial relationships with any commercial interest if the relationship is financial and occurred within the past 12 months. This includes the relationships of spouse/partners. If there are relationships that create a conflict of interest, these must be resolved in accordance with the ACR's CME Resolution of Conflict policy prior to the participation of the individual in the development or presentation of CME content.

This Meet the Professor session has been planned to be well balanced, objective, and scientifically rigorous. Information and opinions offered by the speakers represent their viewpoints. Conclusions drawn by the audience members should be derived from careful consideration of all available scientific information.

Faculty member(s) disclosure is as listed below; related directly to this CME activity. Participants may form their own judgments about the presentations in light of full disclosure of the facts.

## Faculty Disclosure

Paul F. Dellaripa, MD

P. Dellaripa, None

# 005 - Pulmonary Manifestations of Rheumatic Disease

Paul F. Dellaripa, MD

Session Overview:

Lung manifestations are amongst the leading causes of morbidity and mortality in rheumatic diseases. All compartments of the pulmonary circuit can be involved and each rheumatic disease can present with unique features with different prognosis. Appropriate screening and surveillance for pulmonary complications in specific rheumatic diseases should prompt a methodical investigation in conjunction with a pulmonologist. As newer therapies become available for treatment, the rheumatologist can and should play an important role with a dedicated multidisciplinary team to ensure the best outcomes in these most challenging patients.

***Upon completion of this session, participants should be able to*:**

• identify key clinical features associated with lung disease as it presents in specific rheumatic diseases

• outline different prognosis based on pathology, radiographic findings and key clinical biomarkers in lung disease associated with rheumatic disease patient

• determine which diagnostic tests and treatments are appropriate in selected patients with ILD associated with rheumatic diseases

• explain the concept of lung dominant autoimmune disease

# Lung Disease in the Rheumatic Diseases:

Paul F Dellaripa MD
Associate Professor of Medicine
Harvard Medical School
Division of Rheumatology
Co-Director Interstitial Lung Disease Clinic
Brigham and Women's Hospital
Boston MA
2016

## Financial disclosures

- Up to Date
- Boerhringer Ingleheim

## Key Evidence based References


- Park JH, Kim DS, Park IN et al. Prognosis of fibrotic interstitial pneumonia :idiopathic versus collagen vascular disease related subtypes. Am J Resp Crit Care Med. 2007;175(7):705-11
- Tashkin DP et al. Cyclophosphamide versus placebo in scleroderma lung disease. N Eng J Med 2006;354:2655-66
- Solomon JJ, Chung JH, Cosgrove GP. Predictors of mortality in RA associated ILD. Eur Resp J 2016:47(2):588-96
- Gochuico BR , Avila NA, Chow CK et al. Progressive preclinical interstitial lung disease in rheumatoid arthritis Arch Int Med 2008;168(2):159-66
- Tashkin DP, Roth MD Clements PJ, SLSII. Myocophenolate mofetil versus cyclophosphamide in scleroderma related interstitial lung disease Lancet Resp Med 2016:4(9):708-19
- Doyle T, Dellaripa PF, Batra K et al Functional Impact of a Spectrum of Interstitial Lung Abnormalities in Rheumatoid Arthritis Chest 2014;146(1):41-50
- Oldham JM, Adequnsoye A, Valenzi E et al. Characterization of patients with interstitial pneumonia with autoimmune features Eur Resp J 2016:47(6):1767-75


## Objectives of this discussion

- Understand key clinical features to help diagnose specific rheumatic diseases in patients you evaluate with ILD
- Understand which diagnostic tests and treatments are appropriate in selected patients with ILD associated with specific rheumatic diseases, especially in early disease
- Understand the concept of ILD with autoimmune features
- Understand emerging diagnostic and treatment options including anti-fibrotic therapy in ILD with rheumatic diseases

## Why is Lung Disease in the Rheumatic Diseases Important ?

- Incidence is not uncommon
- Undetected disease may progress and result in substantial morbidity and mortality
- Patients are increasingly aware of these complications
- Aggressive treatment can be beneficial and potentially life saving
- Conversely, ILD may predate onset of Rheumatic Disease

## 2 common scenarios

- Scenario I Rheumatologist sees pts with known or suspected CTD and the pt has c/o dyspnea. They think they hear crackles. They order PFTS and a CT scan and call a pulmonary consult.
- Scenario II: Pulmonologist sees a patient with parenchymal lung disease. They order an ANA and its +. The pulmonologist calls a rheumatology consult.

## Which diseases are most likely to lead to interstitial lung disease?

- Scleroderma *
- Dermatomyositis/Polymyositis *
- Rheumatoid arthritis *
- Mixed connective disease
- Sjogrens syndrome
- SLE

## A good history in a pt with ILD

- RA: inflammatory arthritis,pleuritis
- Scleroderma:Raynauds, GERD, limited oral aperture, calcinosis, skin thickening
- IIM: proximal muscle weakness, rash, diff swallowing
- Sjogrens: sicca complex, parotid swelling
- SLE: oral ulcers, pleurisy, rash, arthritis, hair loss
- Exposure: occupational or hobbies and birds.

## Lung Disease patterns: all can be seen in CTD

- UIP
- NSIP: cellular and fibrotic
- LIP (lymphocytic Interstitial Pneumonia)
- COP (BOOP)
- DAD ( Diffuse Alveolar Damage)
- Airway/Bronchiolar disease
- Vasculitis and ILD (ANCA)

## ILD in the CTD: Histology

- Heterogeneity of pts both in disease and pathologic lesions
- RA: UIP>NSIP
- Scleroderma: NSIP>UIP
- IIM: NSIP> OP >UIP

## Pitfalls in understanding ILD in CTD

- We still don't have a firm handle on the natural progression of ILD in CTD compared to IPF and how to measure it ( ie physiologic parameter like FVC or other or a combination of parameters)
- We are still struggling to identify those patients at highest risk for progression and thus deemed best suited for treatment and to enrich prospective trials
- We do fewer lung biopsies than before
- We rely on CT scans to infer histology

## Common tests and metrics at your disposal: diagnosis, prognostication and response to therapy

- FVC
- DLCO
- 6 min walk test
- HRCT
- Echo
- Health quality assessment and patient reported outcomes
- **Remember the tools we use to make a diagnosis and prognosticate are not necessarily the same tools that are the best metrics to measure outcomes in a clinical trial**

## OMERACT in CTD/ILD (

Saketkoo et al Thorax 2014 and Khanna et al J Rheumatol 2015)

- HRCT scoring systems (maximum fibrosis scores in zone of max disease, TLI and computer aided quantification)
- Physiologic (% predicted decline FVC)
- Cough
- Dyspnea scales
- HRQoL
- What about composite indices and will they vary in different CTD?

## Forced Vital Capacity (FVC)

- Probably the most reliable single measure to assess disease progression in ILD
- Typically expressed as a % predicted with >10% *relative* change considered a threshold that indicates meaningful change.
- 2011 IPF guideline: a *relative* decline of 10% from absolute measured values (2.0 to 1.8 litres) = disease progression in the absence of an alternative explanation
- **There is not agreement on what % decline and over what period of time is considered significant**

## FVC

- Different degrees of decline may be important at different stages of disease.( if you lose 10% of function on top of already more significant disease for example)
- Even losing less than 10% could be significant in some pts
- FVC should not be interpreted in isolation as it depends on known baseline FVC
- What are the effects of other comorbid lung disease on FVC (i.e. emphysema or other concomitant pathology) ?

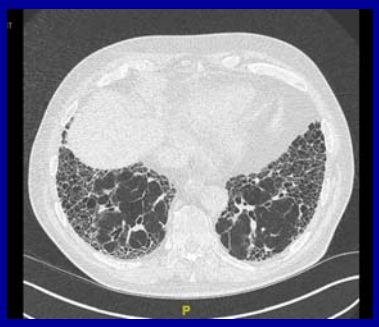
## Other measurements: DLCO and 6 minute walk test

- DLCO confounded by measurement variation and non-specificity especially in scleroderma where there may be concomitant PAH *but may serve as part of a composite index with lower levels of FVC change.*
- Six minute walk distance not validated in a scleroderma cohort and can be difficult to do in scleroderma (perfusion, joint and muscle disease) and in RA ( joint and muscle disease)

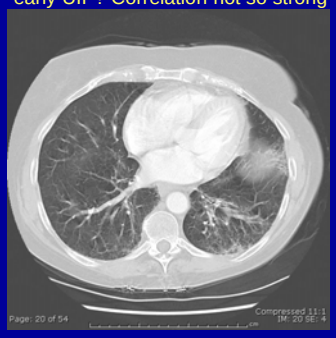
## Histology and the way we define it

- Do we define histology based on CT or by biopsy?
- UIP
- NSIP ( cellular vs fibrotic)
- How much does it matter?
- What really counts in disease progression. Is it the disease entity/phenotype or the specific lung lesion

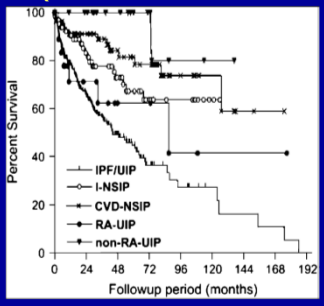
Honeycombing and traction bronchiectasis c/w UIP(specifc but not sensitive)



## Ground glass and reticular changes: Is this NSIP or early UIP? Correlation not so strong




## Comparison:all subject groups in ILD (Park et al Am J Respir Crit Care 2007;175;705)




CHEST
Date of download: 3/4/2015
Copyright © American College of Chest Physicians. All rights reserved.

**From: Pulmonary Function and Survival in Idiopathic vs Secondary Usual Interstitial PneumoniaClinical Context of Usual Interstitial Pneumonia**

Chest. 2014;146(3):775-785. doi:10.1378/chest.13-2388

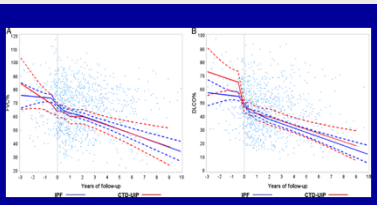



Figure Legend:

**– A, B, Change in FVC% (A) or DLCO% (B) over time for sample stratified on clinical context of UIP. Points represent observed values, with fitted (predicted) functions for groups (blue = IPF, red = CTD-UIP) superimposed; predicted means are solid, 95% confidence bands are dashed. Predicted values were obtained using mixed-model fits, using knots (ie, allowing change points) at −0.5, 0, 0.5, 1, and 2 y from diagnosis. A spatial power covariance structure was included in the model to account for repeated measures within subjects; random effect terms for subjects were also included, as described in e-Appendix 1. There were no significant differences between groups for segments between comparable time points. The plots demonstrate sharper declines near time of diagnosis for both groups. CTD-UIP = connective tissue disease-related usual interstitial pneumonia; DLCO% = % predicted diffusing capacity of the lung for carbon monoxide; FVC% = % predicted FVC; IPF = idiopathic pulmonary fibrosis.**

CHEST
Date of download: 3/4/2015
Copyright © American College of Chest Physicians. All rights reserved.

**From: Pulmonary Function and Survival in Idiopathic vs Secondary Usual Interstitial PneumoniaClinical Context of Usual Interstitial Pneumonia**

Chest. 2014;146(3):775-785. doi:10.1378/chest.13-2388

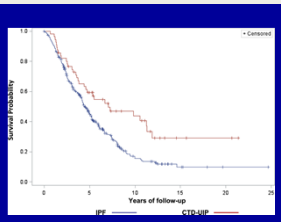


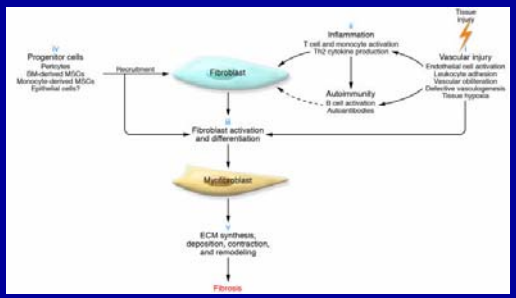

Figure Legend:

**Kaplan-Meier survival curves for sample stratified on clinical context of usual interstitial pneumonia (IPF or CTD-UIP). See Figure 1 legend for expansion of abbreviations.**

TABLE 1 ] Baseline Characteristics of Subjects ( Strand et al Chest Sept 2014)

| Characteristics | IPF (N = 321) | CTD-Related UIP | | | | |
|---|---|---|---|---|---|---|
| | | All (N = 56) | RA (n = 13) | SSc (n = 11) | UCTD (n = 19) | Other (n = 13) |
| Age, y | 66.1 ± 9.1 | 59.3 ± 11.3 | 62.9 ± 10.8 | 59.3 ± 6.9 | 59.5 ± 12.0 | 55.4 ± 13.6 |
| Male sex | 240 (75) | 31 (55) | 11 (85) | 5 (45) | 13 (68) | 2 (15) |
| Ethnicity[a] | | | | | | |
| Non-Hispanic | 294 | 54 | 12 | 11 | 18 | 13 |
| Hispanic | 24 | 2 | 1 | 0 | 1 | 0 |
| Race[a] | | | | 0 | 0 | 0 |
| Asian | 4 (1.3) | 0 | 0 | 1 | 0 | 3 |
| Black | 1 (0.3) | 4 (7) | 0 | 0 | 0 | 0 |
| Other | 2 (0.6) | 0 | 0 | 10 | 19 | 10 |
| White | 311 (97.8) | 52 (93) | 13 | | | |
| FVC % | 71.4 ± 17.4 (n = 315) | 70.6 ± 19.8 (n = 55) | 77.3 ± 16.4 (n = 12) | 85.5 ± 13.5 (n = 11) | 62.6 ± 18.5 (n = 19) | 63.6 ± 21.4 (n = 13) |
| DLCO % | 52.3 ± 18.7 (n = 311) | 54.6 ± 18.2 (n = 54) | 60.7 ± 15.6 (n = 11) | 66.2 ± 22.5 (n = 11) | 42.6 ± 11.8 (n = 19) | 57.0 ± 15.4 (n = 13) |
| Years follow-up | 4.0 (2.1-6.2) | 5.1 (2.6-10.2) | 5.0 (3.1-11.7) | 6.4 (3.3-8.5) | 3.8 (2.4-6.7) | 7.3 (1.8-11.3) |
| Died | 230 (72) | 32 (57) | 7 (54) | 2 (18) | 15 (79) | 8 (62) |

## Scleroderma




## Scleroderma and lung disease

- ILD occurs more frequently in scleroderma than in any other rheumatic disease and is the leading cause of death.
- ILD more frequent in diffuse disease (>50%) but also in limited scleroderma (30%)
- ILD frequently presents within the first four or five years of diagnosis
- ILD In conjunction with pulmonary hypertension implies a worse prognosis.
- Not all ILD Progresses!

## Poorer prognosis in ILD and Scleroderma

- Combination of PAH and ILD
- Scl-70 ab +
- Diffuse skin disease
- Male
- African American or Native American
- Extent of disease on CT(> 20% of HRCT involved) ( TA Winstone et al Chest 2014)
- DLCO less than 40%
- Well's and Goh algorithim ( >20% fibrosis on CT and FVC<70%)

## Goh and Wells(AJRCCM 2008)

- Constructed a prognostic algorithm in SSc-ILD, integrating PFTs and HRCT.
- *Methods*: The prognostic value of baseline PFT and HRCT variables was quantified in patients with SSc-ILD (n = 215) against survival and serial PFT data
- SSc-ILD was staged as limited disease (minimal disease on HRCT or, in indeterminate cases, FVC ⩾ 70%) or extensive disease (severe disease on HRCT or, in indeterminate cases, FVC < 70%). This system (hazards ratio [HR], 3.46; 95% confidence interval [CI], 2.19–5.46; *P* < 0.0005) was more discriminatory than an HRCT threshold of 20% (HR, 2.48; 95% CI, 1.57–3.92; *P* < 0.0005) or an FVC threshold of 70% (HR, 2.11; 95% CI, 1.34–3.32; *P* = 0.001

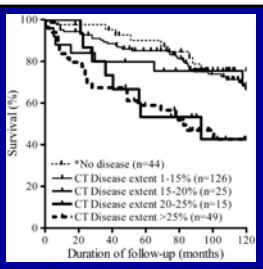



**Figure 2**. Survival is shown in relation to the extent of disease on high-resolution computed tomography (HRCT), illustrating the optimal extent threshold of 20%, as demonstrated by the divergence in outcome in patients with disease extents of 15–20% and 20–25%. Survival did not differ between patients with less than 20% disease extent on HRCT and those with no cardiopulmonary disease. * No disease = no clinical cardiopulmonary disease. CT = high-resolution computed tomography.

Am J Respir Crit Care Med
http://www.atsjournals.org/doi/abs/10.1164/rccm.200706-877OC

Published in: Nicola S. L. Goh; Sujal R. Desai; Sriram Veeraraghavan; David M. Hansell; Susan J. Copley; Toby M. Maher; Tamera J. Corte; Clare R. Sander; Jonathan Ratoff; Anand Devaraj; Gracjela Bozovic; Christopher P. Denton; Carol M. Black; Roland M. du Bois; Athol U. Wells; *Am J Respir Crit Care Med* **2008**, 177, 1248-1254
DOI: 10.1164/rccm.200706-877OC
© 2008 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article inquiries for slides or journals must apply for permission. For permission requests, please contact the Publisher at sgarrigan@thoracic.org or 212-315-6443.

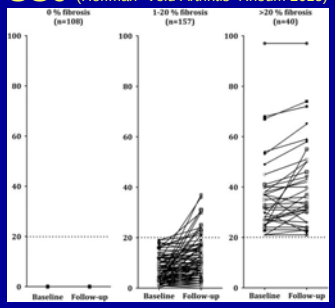

**Figure 1**. Flow diagram of limited/extensive staging system (*A*) with the use of formal high-resolution computed tomography (HRCT) scores, for the purposes of analysis, and (*B*) as applied in clinical practice.

Am J Respir Crit Care Med
http://www.atsjournals.org/doi/abs/10.1164/rccm.200706-877OC

Published in: Nicola S. L. Goh; Sujal R. Desai; Sriram Veeraraghavan; David M. Hansell; Susan J. Copley; Toby M. Maher; Tamera J. Corte; Clare R. Sander; Jonathan Ratoff; Anand Devaraj; Gracjela Bozovic; Christopher P. Denton; Carol M. Black; Roland M. du Bois; Athol U. Wells; *Am J Respir Crit Care Med* **2008**, 177, 1248-1254
DOI: 10.1164/rccm.200706-877OC
© 2008 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article inquiries for slides or journals must apply for permission. For permission requests, please contact the Publisher at sgarrigan@thoracic.org or 212-315-6443.

## Predictive value of baseline CT in SSc (Hoffman -Vold Arthritis Rheum 2015)




## Degree of decline in FVC correlates with degree of fibrosis
(Hoffman -Vold Arthritis Rheum 2015)

**Table 4.** Prediction model with multivariate analyses for lung outcomes in the SSc patients*

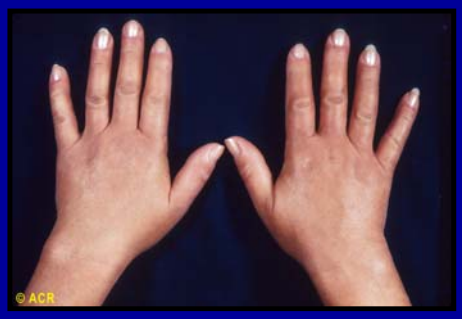
| Variable | Primary outcome: No fibrosis, OR (95% CI)† | P | Primary outcome: Fibrosis >20%, OR (95% CI)‡ | P | Secondary outcome: FVC <70%, OR (95% CI)§ | P | Secondary outcome: FVC decline >10%, OR (95% CI)¶ | P |
|---|---|---|---|---|---|---|---|---|
| Pulmonary hypertension | NS | | NS | | NS | | 2.2 (1.12–4.35) | 0.023 |
| Male sex | NS | | NS | | NS | | NS | |
| Diffuse cutaneous SSc | NS | | NS | | NS | | NS | |
| Anti-topo I antibody | NS | | NS | | NS | | NS | |
| Anticentromere antibody | 4.7 (2.72–7.96) | <0.001 | NS | | 0.3 (0.08–0.77) | 0.017 | 0.4 (0.25–0.73) | 0.002 |
| FVC at baseline | NS | | 1.0 (0.93–0.99) | <0.001 | 0.9 (0.82–0.90) | <0.001 | NS | |
| DLco at baseline | 1.04 (1.02–1.05) | <0.001 | NS | | NS | | NS | |
| Fibrosis at baseline | NS | | 1.3 (1.18–1.36) | 0.045 | 1.0 (1.00–1.08) | 0.049 | NS | |

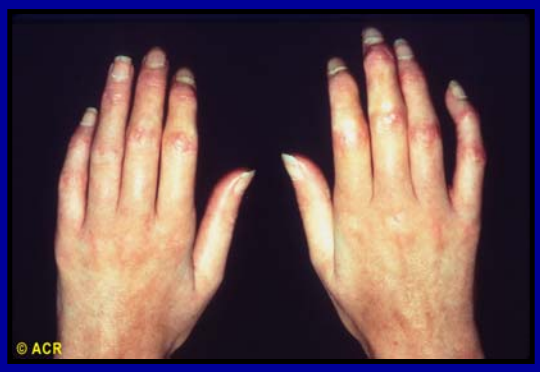
* SSc = systemic sclerosis; OR = odds ratio; 95% CI = 95% confidence interval; FVC = forced vital capacity; NS = not significant; anti-topo I = anti-topoisomerase I; DLco = diffusing capacity for carbon monoxide.
† $P = 0.211$ for goodness of fit; area under the receiver operating characteristic curve 0.78.
‡ $P = 0.511$ for goodness of fit; area under the receiver operating characteristic curve 0.96.
§ $P = 0.434$ for goodness of fit; area under the receiver operating characteristic curve 0.96.
¶ $P = 0.322$ for goodness of fit; area under the receiver operating characteristic curve 0.62.

## SSc antibodies

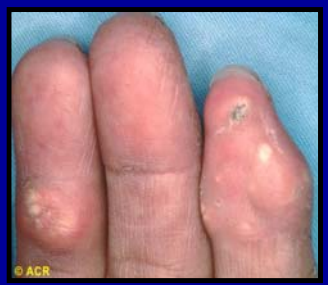
- ANA + in most cases, **nucleolar pattern**
- SCL-70:ILD and diffuse skin 20-30% pts
- Anticentromere pattern : limited SSc, PAH
- RNA polymerase III : increased risk for skin and renal disease, and increased risk for cancer
- Th/To antibody: limited SSc, ILD , PAH
- U1 RNP : mixed disease with overlap with muscle and often see in AA
- U3-RNP: (associated with muscle and lung disease and seen in AA; poor prognosis)

## Puffy hands of early scleroderma

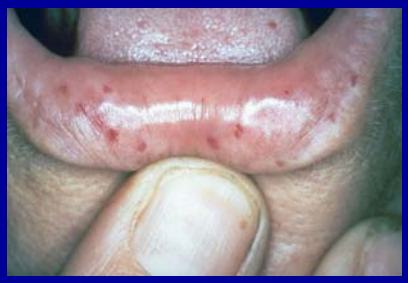


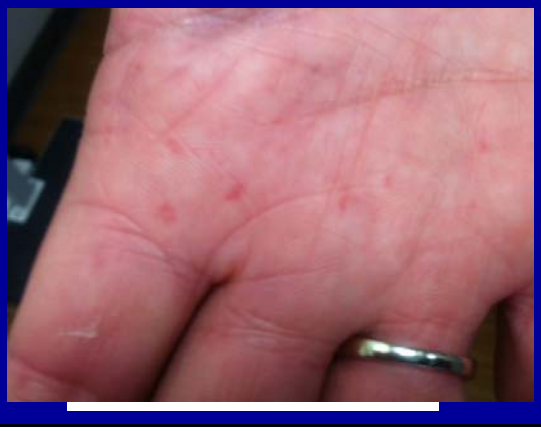




## CREST syndrome: calcinosis cutis, fingers

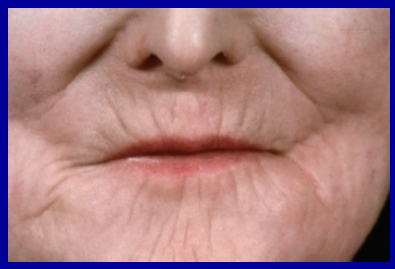


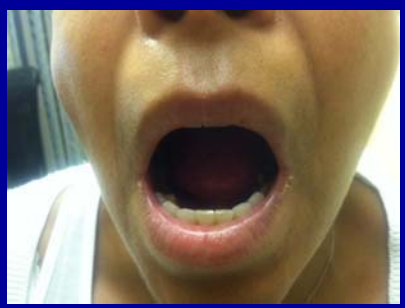
## Telangictasia in Scleroderma



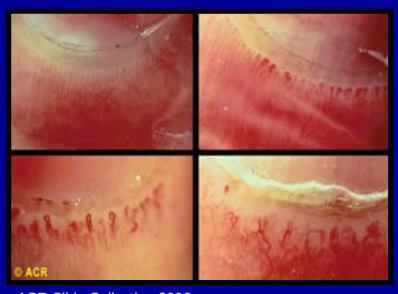


## Limited oral aperture in Scleroderma





Dermatomyositis and scleroderma: periungual involvement (nailfold capillaroscopy)




ACR Slide Collection 2006

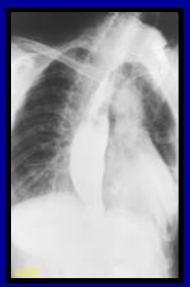
## Raynauds


## Severe Raynaud's with severe ischemia and amputation

## Raynaud's phenomenon

- Primary Raynauds common in young women (teens and twenties), may have a family history of this as well, ANA mostly negative.
- Some of these pts convert to secondary Raynaud's
- **Onset of Raynaud's in adults after the age of 40** *concerning for the development of a rheumatic syndrome* .
- Digital ulcers, pitting scars in fingers, abnormal capillary microscopy and presence of autoantibodies suggest the development of an underlying rheumatic syndrome. (Pavlov Rheumatol Int 2013)
- Why is this important? Some of these patients will develop ILD and or PAH.

## Scleroderma:abnormal motility esophagus



## Aspiration and ILD

- Aspiration related to esophageal dysmotility is common in SSc
- Pts with SSc/ILD had higher levels of acid and nonacid reflux and level reaching the proximal esophagus (Savarino et al Am J Resp CCM 2009:179:408)
- Study utilizing surgical correction of esophageal reflux in IPF pending

- Clinical trials in ILD: Scleroderma

Oral Cyclophosphamide versus Placebo in Scleroderma Lung Disease ( SLS I):Primary Outcomes( NEJM 2006)

- Forced vital capacity was predetermined primary outcome
- FVC predicted improved by 2.53% between treatment group and placebo (p<.03)
- In patients with greater degree of fibrosis, less of a decrement in FVC compared to placebo.

## Cyclophosphamide and Scleroderma (Hoyles RK et al 2006)

- Prospective trial
- IV CYC 6 months followed by AZA for 6 months with prednisone 20 mg on alternate days.
- Trend in improvement in FVC
- *Overall, in Scleroderma, it is difficult to say that CYC offers a significant benefit in terms of lung function or QOL, though CYC still recommended by some rheumatologists and is recommended by EULAR*

## SLS II:mycophenolate vs cyclophosphamide (Clements PJ Lancet Resp Med 2016)

- MMF 3g/d 2yrs vs CYC 2mg/kg for one year
- 106 pt randomized, 2 yr evaluation
- FVC similar in both groups
- Skin scores similar in both groups
- Less bone marrow suppression in the MMF arm

## Role of Autologous Bone Marrow Transplant In Scleroderma

- ASTIS: non-myeloablative BMT vs CYC 750 mg/m2 monthly for 1yr
- Data suggests carefully screened patients with early progressive skin disease who do not have cardiac disease benefit in terms of overall and event free survival in comparison to CYC alone.
- Other trials (SCOT and ASSIST)

## ILD and scleroderma:Summary

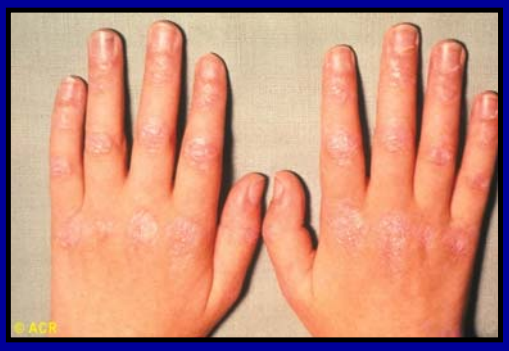
- Majority of patients with scleroderma with ILD likely have NSIP.
- Mycophenolate increasingly utilized based on SLS II
- Azathioprine and Rituximab utilized in ILD
- Antifibrotic agents used in IPF approaching clinical trials (SLS 3 and now as FDA approved orphan drug )
- ? Paradigm shift with bone marrow transplant
- What is the value of GI motility assessment and treatment for chronic reflux?

## Who should we treat?

- >20% fibrosis on HRCT
  - If <20% and FVC <70% then consider treatment (Goh 2008 AJRCCM)
- If yearly decline in FVC >10% or Decline of DLCO (relative) >15% **and** FVC <10% and >5% (OMERACT J Rheumatol 2015 )

## Inflammatory Myositis and the lung

- Respiratory muscle dysfunction
- Diaphragmatic dysfunction
- Interstitial lung disease (UIP, NSIP and Acute interstitial pneumonitis)
- BOOP (COP)
- Pneumomediastinum
- Antisynthetase syndrome (fever, Raynauds, arthritis, myositis, mechanics hands,ILD)

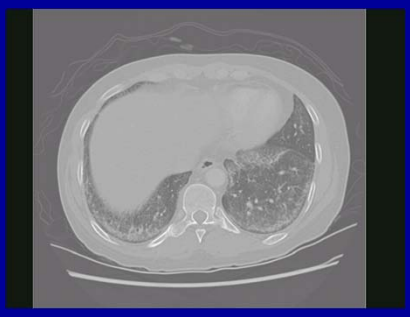



ACR Slide Collection 2006

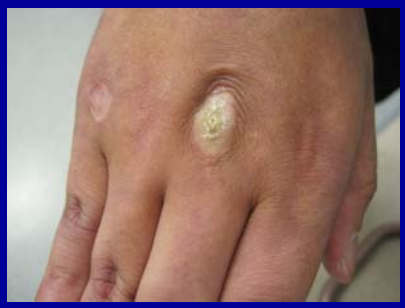
## Erythematous rash in DM

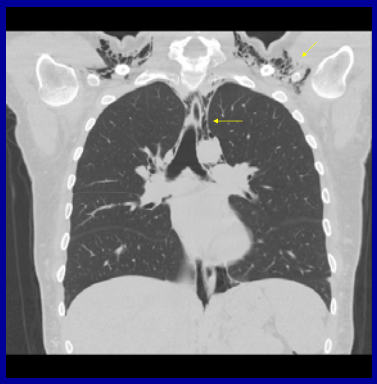

ACR Slide Collection 2006

## NSIP in patient with DM

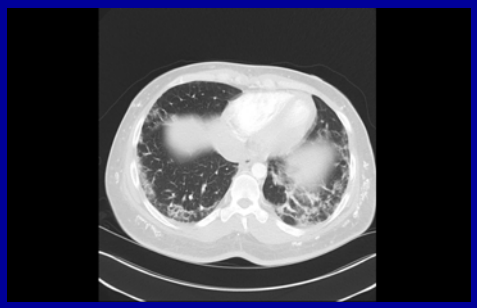


## Vasculopathic lesion seen in DM



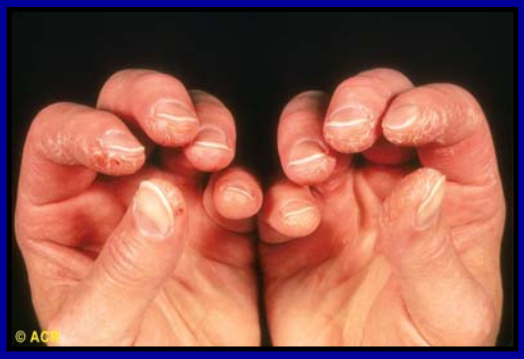


## ILD in DM in same patient with pneumomediastinum

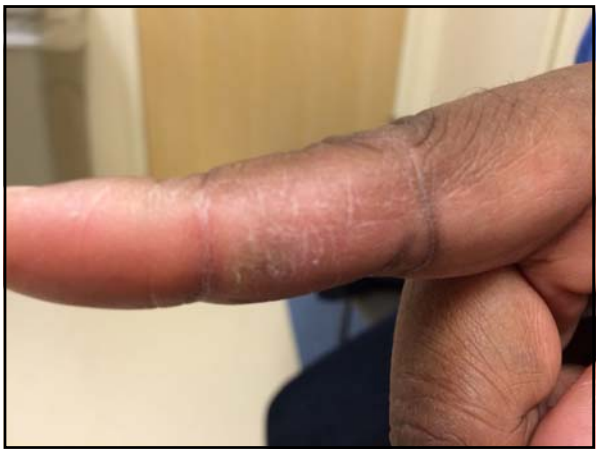


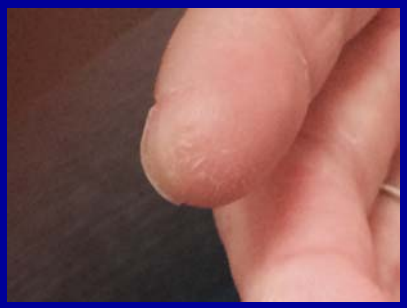
## Antisynthetase syndrome

- Fever
- Raynauds
- Inflammatory Arthritis
- Mechanics hands
- ILD



ACR Slide Collection 2006



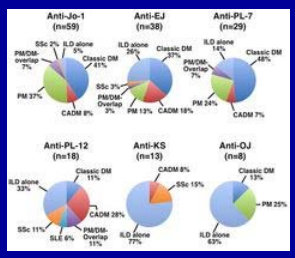


## Antisynthetase antibodies

- Ubiquitous cytoplasmic enzymes that play a key role in protein synthesis
- Auto antibodies against aminoacyl t RNA synthetases occur in 16-28% of patients with myopathy, Jo-1 most prevalent.

## Antibodies in myositis and ILD:summary

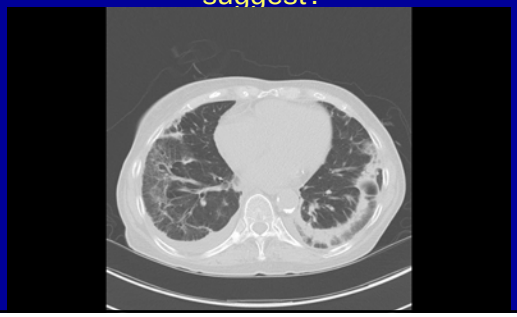
- Antisynthetase abs: Jo-1,PL-7, PL-12, EJ, OJ, KS, ZO , HA.
- Overlap antibodies: RNP, PML/Sc.
- Antibodies associated with malignancy in DM ( p155/140)
- **Amyopathic antibodies**: **anti-MDA5, can result in rapidly progressive ILD**
- **SUMO ab: small ubiquitin-like modifier activating enzyme seen in DM/ILD**



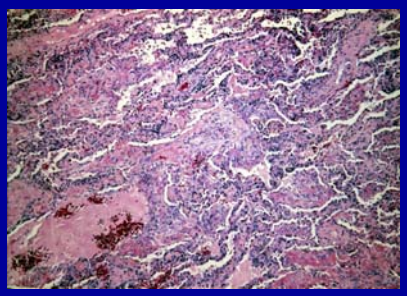

## ILD in IIM or MA ILD:predictors of poorer outcomes

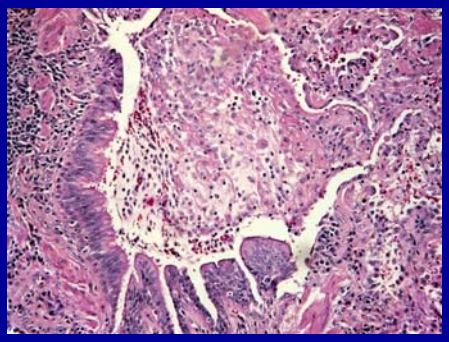
- Acute/subacute form
- Older age onset
- lower level of FVC
- CADM (*Fujisawa 2014 Plos One)
- **Relative decline of 10 and 15% FVC predictive of survival ( Blom et al ACR 2015)**
- **In some ways, detecting ILD may be easier in IIM given that screening for it is so prevalent**

39 yo female with weakness, dyspnea and elevated CK Jo-1+. What pathology does this CT suggest?



## BOOP/COP



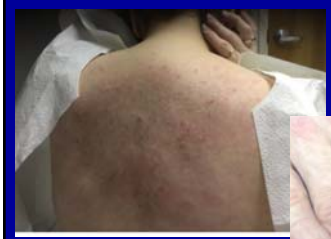


## cryptogenic organizing pneumonitis (COP) or (BOOP)

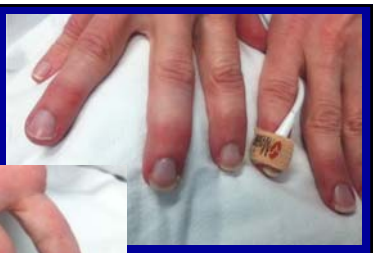
- Characterized by organizing pneumonia and granulation in the distal airways.
- Typically steroid responsive, but treatment involves steroids tapered slowly over 6-12 months
- Sometimes incomplete forms seen, showing only organizing pneumonia
- ? slower recovery compared to idiopathic COP; ***low threshold for DMARD***
- Seen in IIM, RA,, SLE and SSC.
- ***Acute onset of COP in a generally well pt should raise the suspicion/investigation for a CTD***

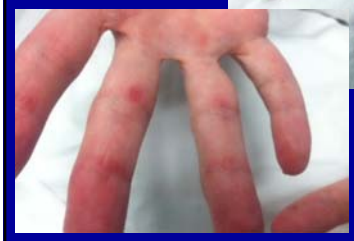
Case:Two months prior to admission

Two months prior to admission

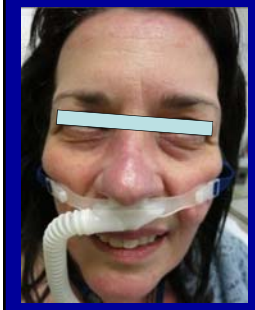


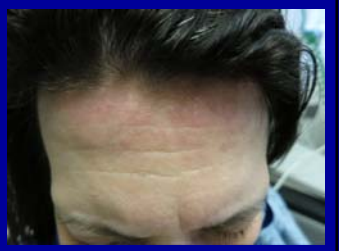
On admission

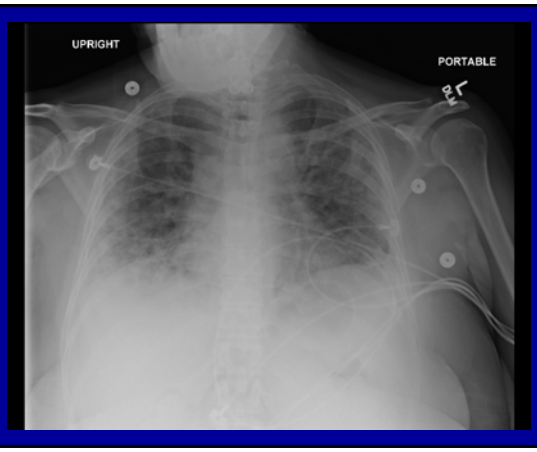


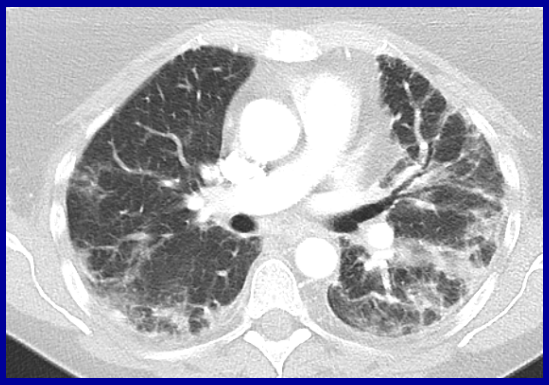


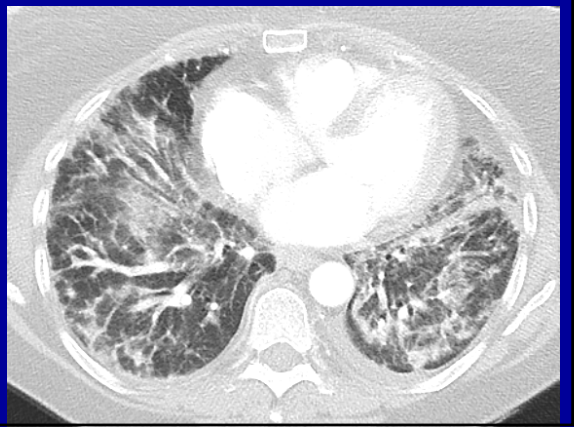
On admission

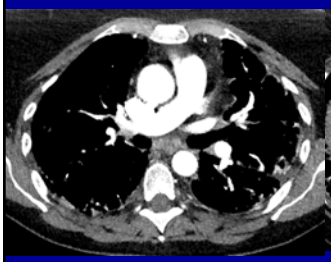


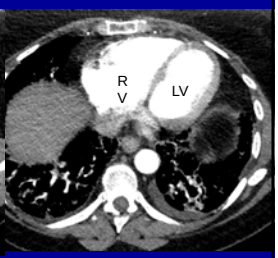


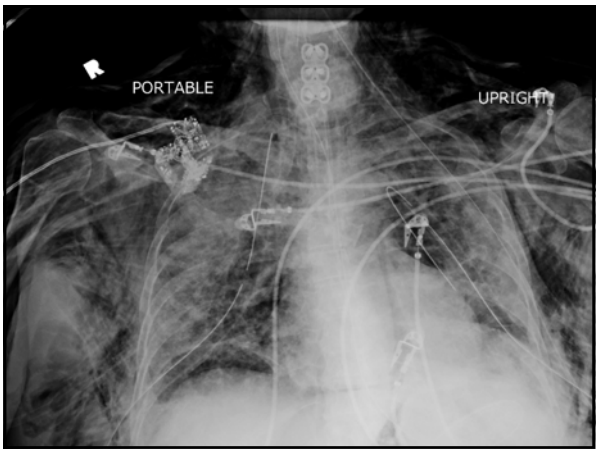






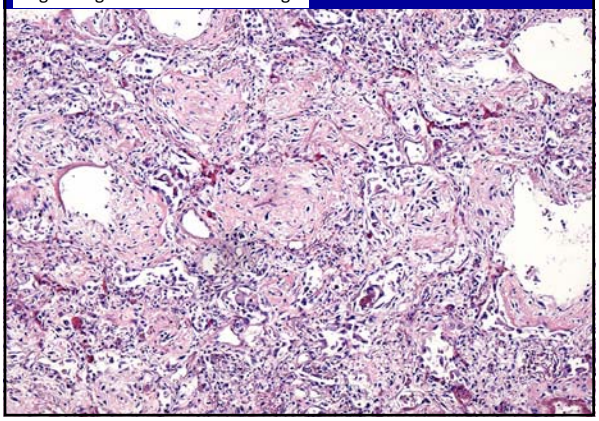




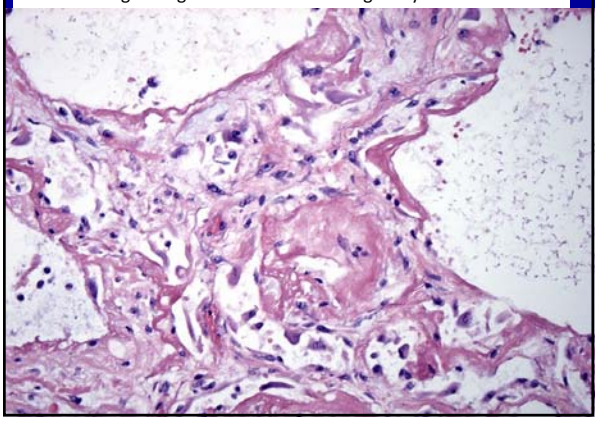

## Differential diagnosis

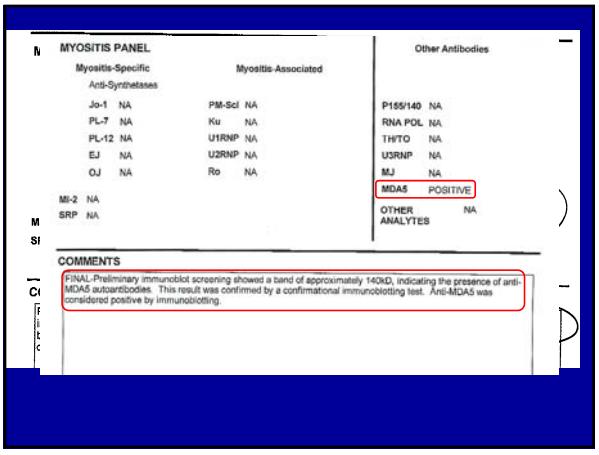
- Underlying autoimmune disease ( dermatomyositis, SLE, UCTD)
- Underlying malignancy associated with inflammatory parenchymal lung disease perhaps organizing pneumonia.
- Pathology obtained (autopsy)

Organizing diffuse alveolar damage



Acute and organizing diffuse alveolar damage – hyaline membranes





MYOSITIS PANEL

| Myositis-Specific Anti-Synthetases | | Myositis-Associated | | Other Antibodies | |
|---|---|---|---|---|---|
| Jo-1 | NA | PM-Scl | NA | P155/140 | NA |
| PL-7 | NA | Ku | NA | RNA POL | NA |
| PL-12 | NA | U1RNP | NA | TH/TO | NA |
| EJ | NA | U2RNP | NA | U3RNP | NA |
| OJ | NA | Ro | NA | MJ | NA |
| | | | | MDA5 | POSITIVE |
| Mi-2 | NA | | | OTHER ANALYTES | NA |
| SRP | NA | | | | |

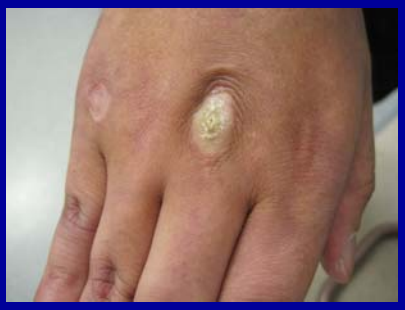
COMMENTS

FINAL: Preliminary immunoblot screening showed a band of approximately 140kD, indicating the presence of anti-MDA5 autoantibodies. This result was confirmed by a confirmational immunoblotting test. Anti-MDA5 was considered positive by immunoblotting.

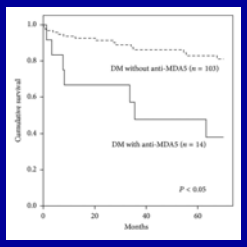
## Anti-melanoma differentiation associated protein 5

- Also known as interferon-induced helicase-1 (IFIH1), is a member of the retinoic acid-inducible gene I-like helicase (RIG-I or RLH) family of proteins, which function by recognizing viral RNA and can induce production of Type I IFN
- Can be associated with dermatomyositis, but often seen in **clinically amyopathic cases (CADM)**
- Distinct cutaneous features include ulcerating lesions, nodular lesions often palmar in location
- RA-like inflammatory arthritis
- In some Asian/European cohorts, **rapidly progressive ILD** noted though mixed findings in NA cohort (Hall et al Arthritis Research 2013 Moghadam Arthritis Research 2015)
- **Could identification of this antibody change treatment plan?**

## Vasculopathic lesion in pt with MDA5



## Prognosis and MDA5 ab (J Immuno Research 2014)




## Treatment of ILD and antisynthetase syndrome/IIM: What to do? (Eminence based)

- Corticosteroids: in combination with a second agent; don't taper steroids too fast !
- Cyclophosphamide: rapidly progressive disease
- Mycophenolate and AZA
- Tacrolimus: case reports but encouraging signal
- Rituximab: small case studies ?signal in antisynthetase syndrome
- ?abatacept
- Multiple agents in combination (CYC, CS and calcineurin inhibition)

*Final points on ambiguous cases:teaching points for your pulm/CCM colleagues*

- In the setting of inflammatory skin lesions and interstitial lung disease, an autoimmune process such as DM , antisynthetase syndrome, SLE perhaps APS needs to be considered
- Try to get the Pulm/CCM to call a rheumatologist sooner; don't wait for the antibodies to come back
- The presence of the MDA5 ab is suggested by rather distinctive cutaneous lesions and potentially a progressive and fatal ILD

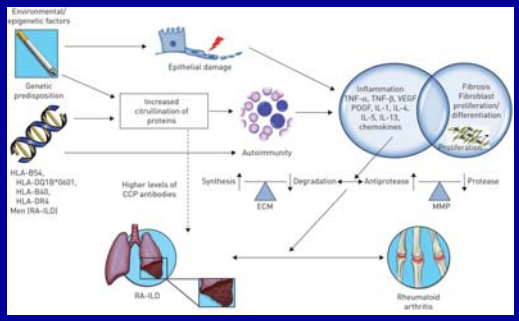
## Rheumatoid Arthritis and the Lung

- Clinically significant interstitial lung disease occurs in 8-14% (NSIP, UIP, LIP and CIP).
- Obstructive bronchiolitis ( poor prognosis)
- Follicular bronchiolitis (better prognosis)
- Cryptogenic organizing pneumonia( formerly known as BOOP, better prognosis)
- Pleural effusion/sterile empyema
- Emphysema
- Nodulosis
- Upper airway obstruction
- Methotrexate toxicity (<1%)
- Leflunomide lung toxicity and for that matter virtually any DMARD/biologic

# RA:Points to consider in RA ILD for the practicing rheumatologist

- As a rheumatologist, a select group of RA patients that we have will develop lung disease and some will develop progressive lung disease that will result in increased morbidity and mortality
- Can we identify who is at risk for ILD and then moreover who is at risk for decline?
- If we can identify those pts, what are the tools we have at our disposal to measure their progression and decline
- But before we discuss that, let's review some basic concepts and potential phenotypes that not only challenge our ability to detect patients that have ILD but also determine which pts are likely to be suitable for clinical trials ( i.e who have progressive disease)

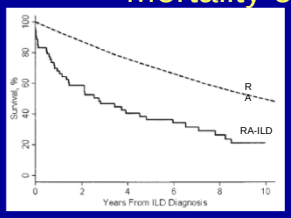
**Schematic illustration of the concepts in the pathogenesis of rheumatoid arthritis associated-interstitial lung disease (RA-ILD**

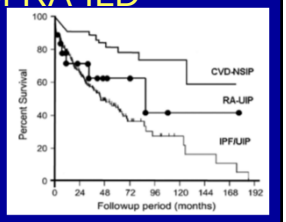



**Megan Shaw et al. Eur Respir Rev 2015;24:1-16**

©2015 by European Respiratory Society

# Mortality of RA-ILD

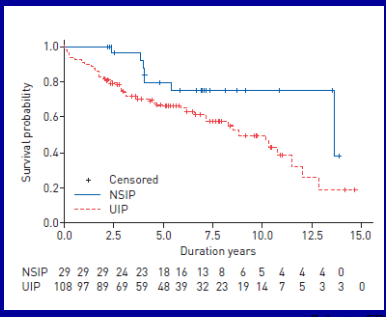



- **While overall mortality rates for RA are declining, death from RA-ILD has increased**
- **Survival in RA-UIP resembles that of IPF**

**Olson AJRCCM 2011**
**Bongartz Arth Rheum 2010**
**Park AJRCCM 2007**
**Kim Chest 2009**

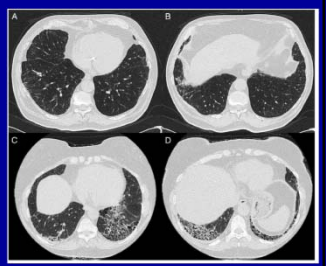
# Solomon JJ Eur Resp J 2016




Solomon ERJ 2015

# Spectrum of ILD in RA

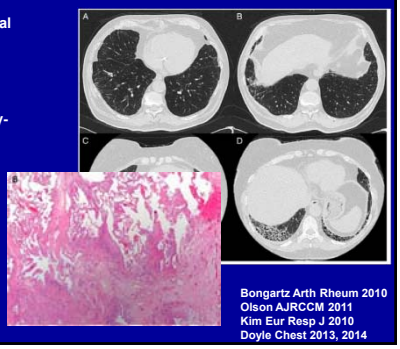
- **Most common clinical manifestation of lung involvement**
- **10% of individuals with RA have clinically-evident ILD and an additional 30% have subclinical disease**




**Bongartz Arth Rheum 2010**
**Olson AJRCCM 2011**
**Kim Eur Resp J 2010**
**Doyle Chest 2013, 2014**

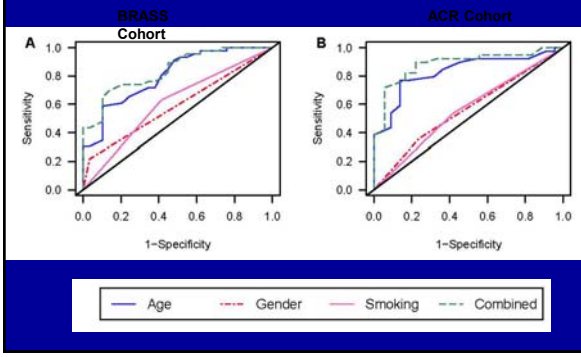
# Spectrum of ILD in RA

- Most common clinical manifestation of lung involvement
- 10% of individuals with RA have clinically-evident ILD and an additional 30% have subclinical disease
- Up to 65% of individuals have UIP pattern

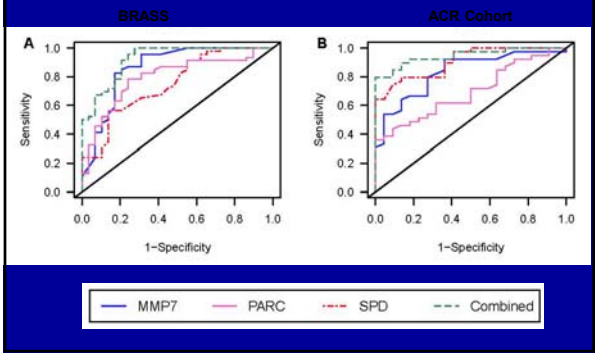


Bongartz Arth Rheum 2010
Olson AJRCCM 2011
Kim Eur Resp J 2010
Doyle Chest 2013, 2014

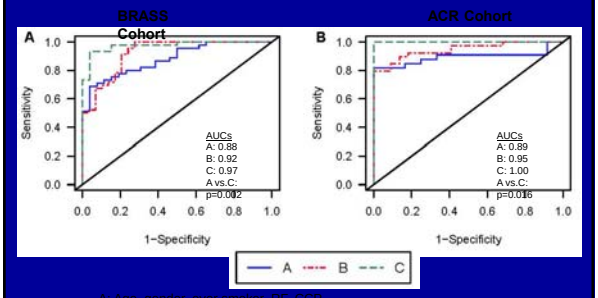
# Demographics are Strongly Associated with the Presence of RA-ILD




# Biomarker Signature is Strongly Associated with the Presence of RA-ILD

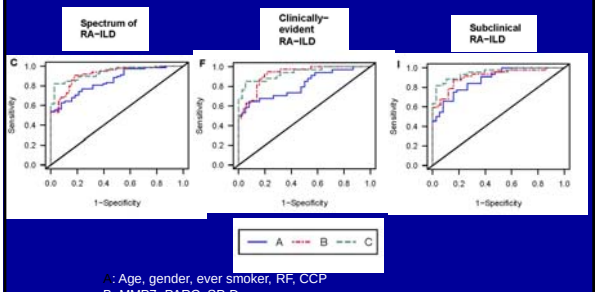



# Biomarker signature in combination with clinical criteria increases ability to detect RA-ILD




A: Age, gender, ever smoker, RF, CCP
B: MMP7, PARC, SP-D
C: Age, gender, ever smoker, RF, CCP, MMP7, PARC, SP-D

# Combinatorial Signature in the BRASS and ACR Combined Cohorts




A: Age, gender, ever smoker, RF, CCP
B: MMP7, PARC, SP-D
C: Age, gender, ever smoker, RF, CCP, MMP7, PARC, SP-D

# Diagnostic Test

- Formula for the identification of subclinical RA-ILD in the derivation cohort:

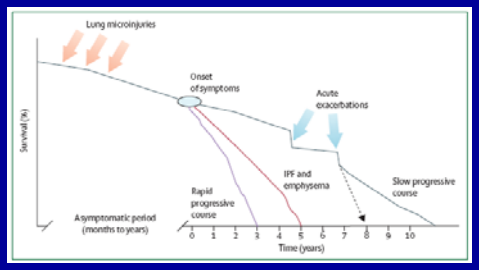
  Risk score = 0.38*Age - 6.4*Gender - 2.3*Ever smoker - 0.0005*RF + 0.0026*CCP + 0.65* MMP7 + 0.15*SPD + 0.024*PARC

- Cutoff with the optimal combination of sensitivity and specificity was 28.2

## A Diagnostic Test ( or a screening test?)

- This algorithm correctly identified subclinical RA-ILD in validation cohort.
  - Sensitivity of 0.87 / Specificity of 0.92
  - Positive likelihood ratio of 10.4 / Negative likelihood ratio of 0.15
  - Based on a prevalence of 30%, the positive predictive value is 84% and negative predictive value is 94%

## Natural History of UIP(IPF): Does this apply to UIP/CTD?




Selman Lancet 2011



## RA and ILD

- ILD in RA may develop prior to or at the time of articular RA, or years after the diagnosis of RA..
- Predicting progression in ILD associated with RA is more challenging than in IPF
- Genetic and environmental determinants ( i.e. smoking ) are potential disease modifiers that influence outcomes
- Risk/predictor profile involving *age, gender,RF/CCP status, smoking hx, molecular phenotyping gene expression and proteonomics of pts with ILD is in progress*.
- **Are we ready to screen for ILD in RA ?**

## RA and the lung

- ILD and co-existent Emphysema are common
- PANTHER trial :immunosuppression (AZA/CS) resulted in higher mortality in IPF (NEJM 2012)
- Is UIP in RA like UIP in IPF and what is the relationship to PANTHER ( where DMARDS in IPF resulted in a worse prognosis)
- What role do new antifibrotic therapies for IPF play in RA UIP?

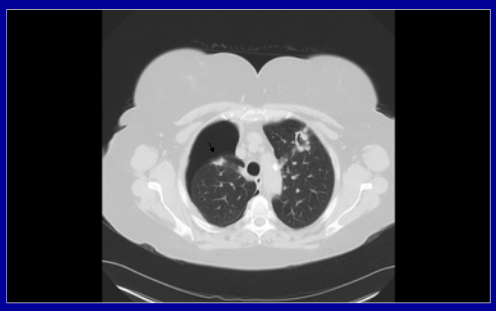
## Bronchiectasis in RA

- ? Extra-articular manifestation of RA
- Pulmonary complications common in these patients
- Cautious use of immunosuppression including biologics in this group of patients
- Not an exclusion criteria in many trials

## Pulmonary Nodulosis in RA

- Not uncommon in RA
- May increase with the use of MTX
- They can become infected and develop bronchopleural fistula
- What is the treatment?

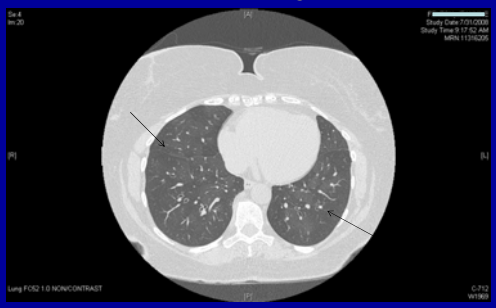
## Pneumothorax due to ruptured rheumatoid nodule



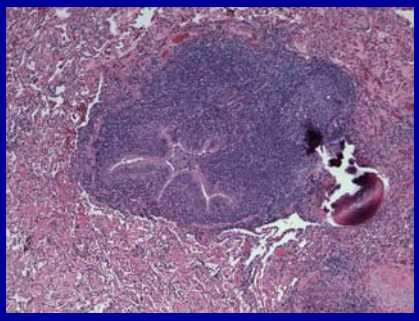
## Airway Disease in RA

- Airway disease with predominantly obstruction on PFTs ( FEV1<70%, ratio FEV1/FVC<) is not uncommon
- May mimic asthma
- Look for mosacism or air trapping on CT
- Some types of bronchiolitis are potentially treatable though OB ( obliterative bronchiolitis) is not and requires referral for transplant.

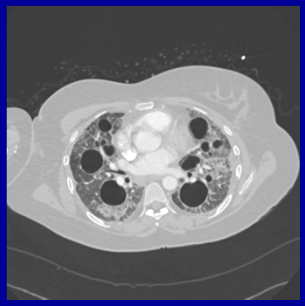
## RA pt with recurrent cough, worse obstruction on PFTs thought to be asthma



## Case

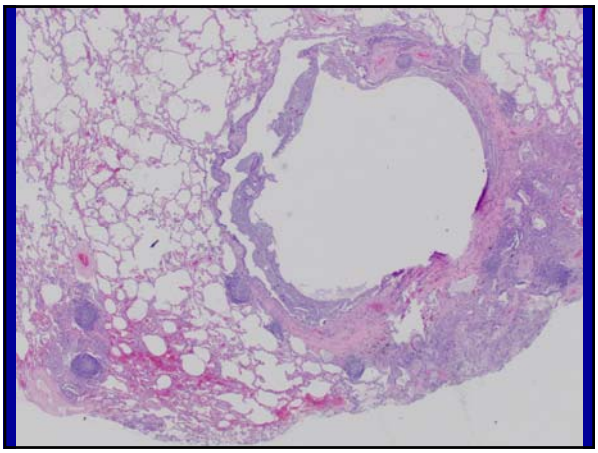


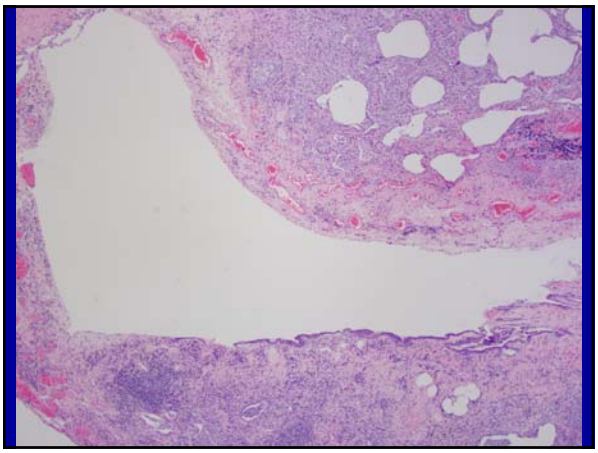
## RA pt with multiple thin walled cysts and GGO with worse DOE

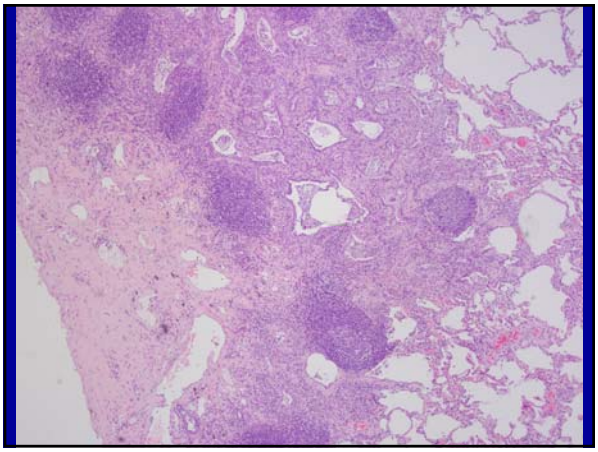


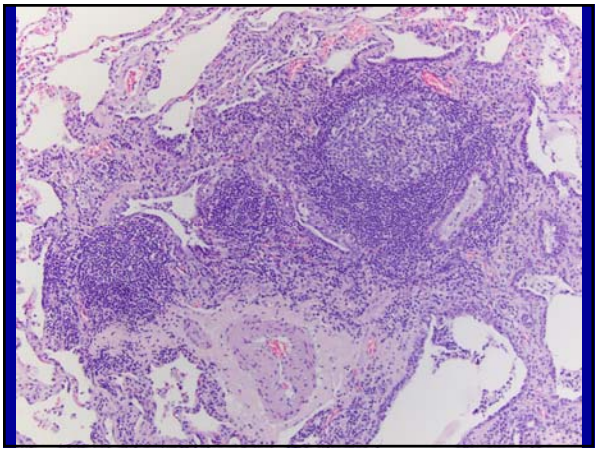
## A VATS biopsy was done by the outside referring MD

- Path reading at local institution:
- **May 2016 :subpleural fibrosis, honeycomb and fibroblastic foci, lymphoid aggregretes, focal organizing pneumonia.**
- **This was thought to be most c/w UIP in the context of RA**
- **She was started on 40 mg of prednisone and MMF was started.**
- **The biopsy was reviewed**





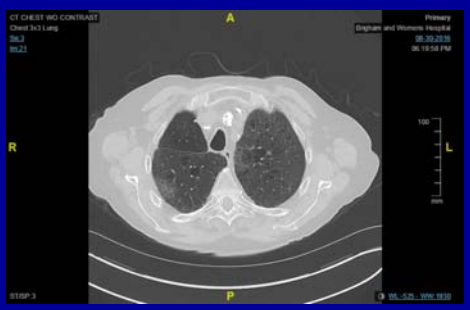




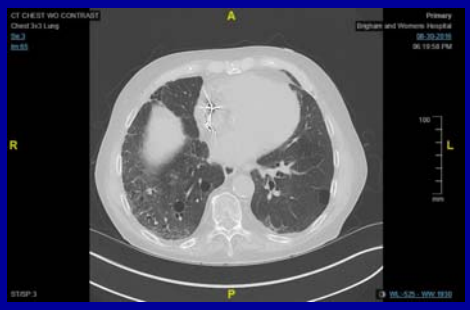
## Causes of Cystic Lung Disease

- Centrilobular emphysema
- Lymphangioleiomyomatosis (LAM)
- Langerhans cell histiocytosis
- ***Lymphoid interstitial pneumonia** ( Sjogrens , RA, SLE ,SSc)***
- Pulmonary metastases (squamous/adenocarcinoma)
- Cystic fibrohistiocytic tumour of the lung
- Subacute (± chronic) hypersensitivity pneumonitis
- Barotrauma/ARDS
- Pulmonary infection—pneumatocoeles
- Desquamative interstitial pneumonia
- Necrobiotic nodules (end stage)
- Birt Hogg Dubé syndrome
- Tracheal papillomatosis
- Cystic mesenchymomas
- Light-chain disease

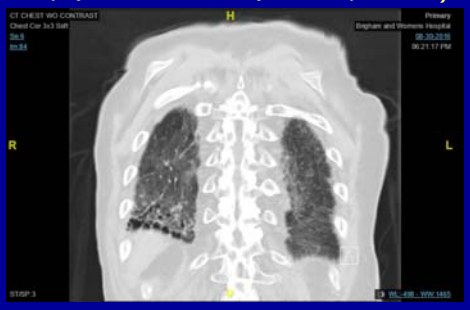
## Pt JC



## Pt JC



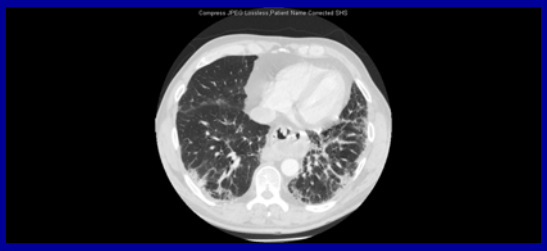
## Pt JC: likely with 3 pathologies ( centrolobular emphysema, LIP with cysts and prob UIP)



## BH: RA ILD Phenotype I

- 55 yo male developed relatively sudden onset of dyspnea on exertion December 2014
- 20 pk yr smoking , quit 20 years ago
- He notes joint pain in his left wrist and shoulders in January 2015
- we met him in ILD clinic late April 2015

## CT BH April 2015



## Initial evaluation

- Laboratory evaluation showed high titer RF and CCP ab
- All other evaluation negative
- Given what looked like mostly OP ( organizing pneumonia) on CT, we elected to start him on high dose steroids and consideration for Rituximab for his RA,pending insurance approval.

## PFTs: started high dose steroids in May

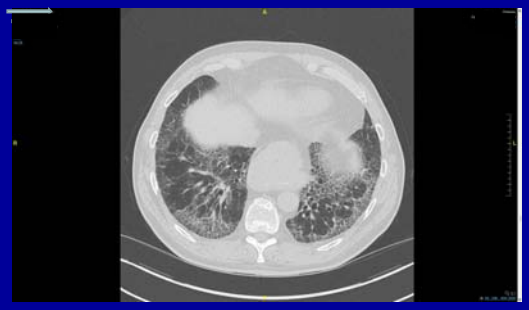
**March 2015**

- FVC 80%
- TLC 74 %
- DLCO 66 %

**July 2015**

- FVC 75%
- TLC 67%
- DLCO 54 %

## CT BH July 2015



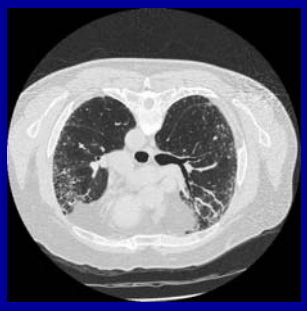
## BH:Phenotype I:Lessons learned

- Rapidly progressive ILD does occur in RA
- PFTs can be deceiving or may not fully reflect the pathologic decline and remodeling that may occur either on CT or by biopsy
- Began Rituximab in August
- Now beginning transplant evaluation
- He is probably a better candidate for a clinical trial using antifibrotic therapy

## Pt JH:Phenotype II

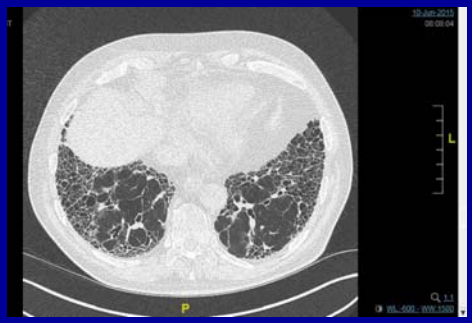
- 67 yo who presented to ILD clinic in 2010 with known fibrotic lung disease since 2006 with mild clinical symptoms. (FVC 93% DLCO 60%)
- In retrospect, he had abnml CXR 2002.
- 15 pk yr smoke quit at age 30.
- Lung bx 2009 showed UIP, thought to have IPF.
- Went on a CO trial

## Pt JH:Phenotype II:2006



## Pt JH

- In 2013 represented with swollen hands,
- CCP and RF high + (RF previously negative in 2009, CCP not checked )
- Started on MMF and Abatacept for joint disease (he declined RTX)
- Pt cont to decline on 6 L oxygen and in 2015 on active transplant list ( FVC 87% DLCO 29%)



## Lessons learned from this case

- This pt likely had ILD dating back 2002 and now he is still alive in 2015
- Is this really IPF or **ILD where ILD preceded RA in joints** ?
- PFTs show a decline in DLCO, not FVC.
- He had a slow decline and then a punctuated decline late in his course
- He may have been a good candidate for a clinical trial with antifibrotic therapy.

## Interstitial Pneumonia with autoimmune features (Fischer et al Eur Resp J 2015 )

- 3 domains notable :Clinical, serologic and morphologic ( path, CT and physiology)
- Disease is limited mostly or exclusively to the lung with specific pathologic features ( NSIP, UIP, OP, DAD or DIP)
- Autoantibodies
- Specific path features inc lymphoid aggregates, extensive pleuritis, perivascular collagen or prominent plasmacytic infiltration
- Other systemic features may follow (or not)

## Sjogren's syndrome and ILD (Parambil et al Chest 2006:1489)

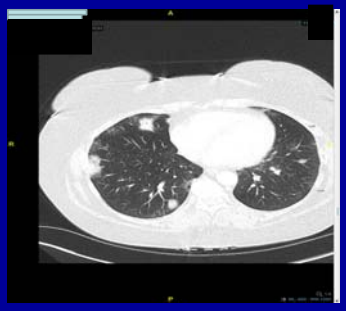
- NSIP
- UIP
- LIP
- COP
- amyloidosis
- Lymphoma

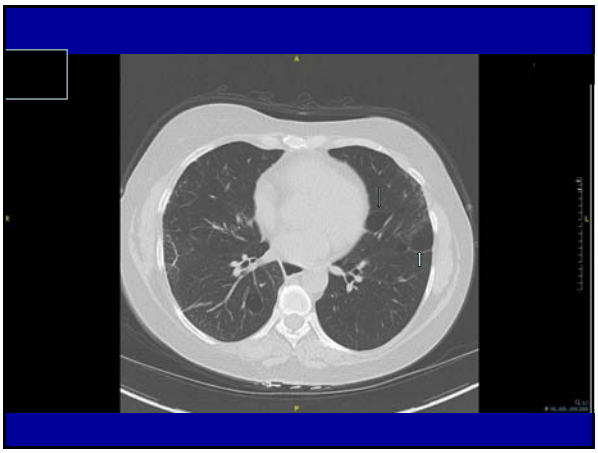
## Case KB: Sjogrens

- 58 yo female with longstanding UCTD/?SLE with sicca complex and new parotid mass

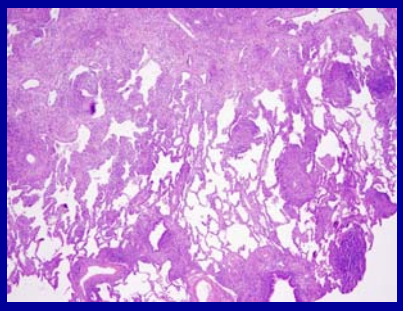
## Case KB

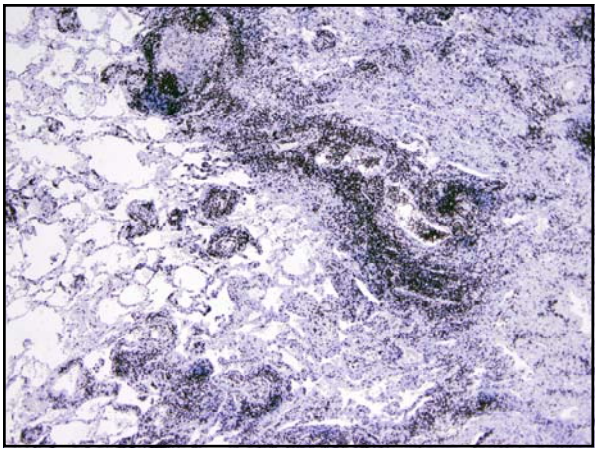
- During the evaluation, lower cut of neck CT imaging showed a lung nodule and some inflammatory lung disease and a dedicated CT was done.



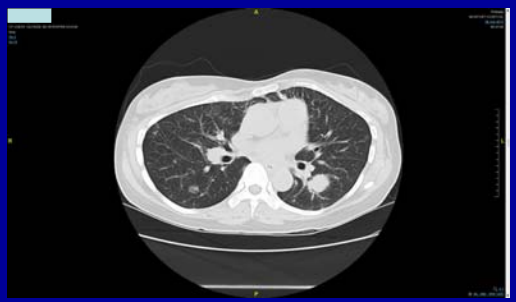


## Lung bx 9/2014 c/w LIP





50 yo with known SS with 8 lb wt loss but lung biopsy this time showed marginal zone lymphoma



## Lung disease and SS

- All forms of ILD are described but are rare.
- NSIP, LIP , UIP ,OP.
- Functional deterioration is unusual but has been described.
- *Major concern is where there is focal nodular lesion, does that represent lymphoma and in rare cases amyloidosis which may require biopsy*.

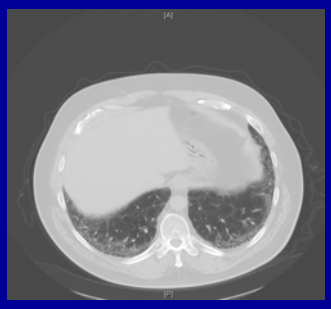
## Mixed and Undifferentiated Connective Tissue Disease

- Typically RNP ab +
- Pulmonary dysfunction in up to 80% patients,
- Patients may evolve into SSC, SLE, RA and PM/DM
- In one prospective study , diminished DLCO noted in 72% with ILD noted in approximately 21% of patients.
- These people need to followed for development of ILD and PAH

## SLE and the lung

- ILD not common
- Pleuritis and pleural effusions
- Diffuse alveolar hemorrhage
- COP/BOOP
- Acute interstitial pneumonitis
- Pulmonary veno-occlusive disease
- Shrinking lung syndrome

50 you with dry cough for 1.5 years, ?IPF presented to ILD clinic:recurrent sinusitis

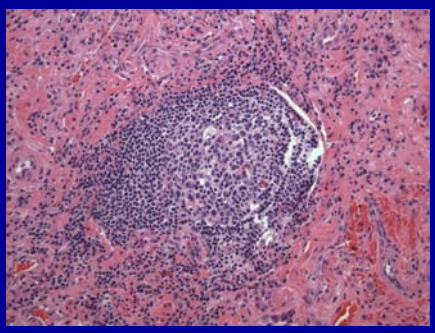


## What to do?

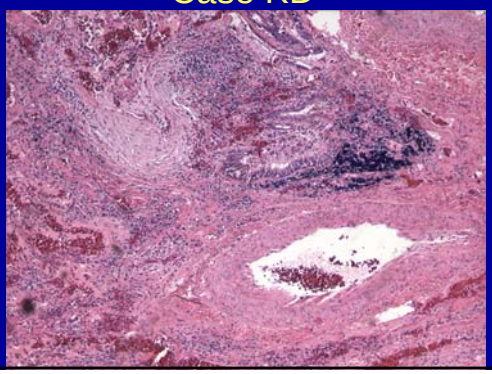
- Sinus biopsy: nonspecific inflammation
- Gram stain negative, AFB negative
- No granulomas, no vasculitis
- pANCA + MPO high titer

- ?lung biopsy

## Case KD



## Case KD



## Case

- There is extensive chronic inflammation, lymphoid follicles formation, fibrosis, and organization.
- The lymphoid follicles stain centrally with CD20.
- Overall, the findings are that of interstitial fibrosis and pneumonitis with features consistent with UIP
- Rx with Rituximab and MMF, Pirfenidone

## ANCA associated ILD: Does it exist and if so what is it?

- Yes, it does exist.
- WGET Trial:7.2 % of patients had fibrotic lung disease, attributed perhaps to vasculitis (Seo et al. Arthritis Rheum 2005:2168)
- In a retrospective analysis of 49 pts, a combination of pulmonary fibrosis and AAV had a poor prognosis. (Comarmond et al Medicine 2014)

## Summary: How aggressive to screen in CTD for ILD and whom?

- Scleroderma patients require the most aggressive evaluation for lung disease followed by PM/DM and then MCTD and RA
- **Scleroderma**:CT and Echo/PFTs baseline)
- **IIM**: Baseline PFT/CT and especially in antisynthetase patients.
- **RA**: probably a risk factor analysis in combination with a functional test will determine who gets PFT/CT scanning.

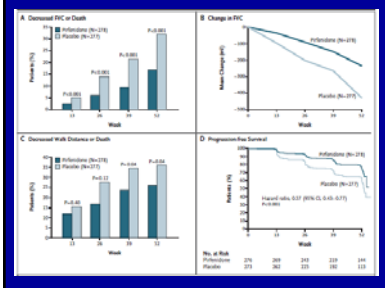
## Serum biomarkers in ILD

- KL-6 and surfactant protein D: glycoproteins expressed by Type II pneumocytes
- MMP7 (Rosas et al PLoS Medicine 2008)
- Pulmonary and Activation Chemokine ( TJ Doyle et al AJRCCM 2015)
- Very interesting and getting close to clinical utility.

## *ILD in the CTD: a new paradigm and implications for treatment*

- When the predominant lung lesion is inflammatory, then anti-inflammatory therapy is indicated
- When the predominant lung lesion is fibrotic, then anti fibrotic therapies are indicated

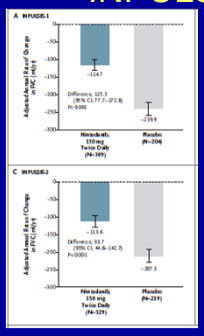
## ASCEND trial



- ASSessment of pirfenidone to Confirm Efficacy aND safety in IPF
- 555 subjects: pirfenidone (2403 mg/day) vs. placebo for 52 weeks
- Significant reduction in rate of decline of FVC and 6MWD and improved progression-free survival

King NEJM 2014

# INPULSIS-1 and -2



Annual Rate of Decline in FVC

- 1066 patients: Nintedanib 150mg BID vs. placebo for 52 weeks
- Demonstrated lower annual rate of decline in FVC.
- INPULSIS-2 demonstrated increase in time to first exacerbation

Richeldi NEJM 2014

# DMARDS/Biologics in CTD pts with ILD

- TNF inhibition can cause Granulomatous formation in lungs
- TNF inhibitors should be used cautiously in pts with pre-existing ILD
- In large series, conflicting data on role of TNFs in either initiating ILD or exacerbating preexistent ILD {(Perez Sem Arthritis 2011 Oct 41(2):256 (YES) and Dixon et al Ann Rheum Dis 2010 69(6):1086-91 (NO)}
- Virtually all drugs used in CTD may cause an inflammatory reaction in the lungs.
- **Given PANTHER data in IPF, is utilizing DMARDS like MMF in UIP/CTD ILD a problem?**

# Treatment Options in ILD

- Mycophenolate increasingly utilized up to 3 g per day
- Cyclophosphamide:, likely useful in severe inflammatory disease such as seen in IIM, Modest benefit in fibrotic disease as noted in Scleroderma lung study
- B cell targeted therapy (rituximab) Arthritis Res Ther. 2010;12(2):112. : utilized in SSc and in some cases of IIM
- Azathioprine, tacrolimus stem cell transplant
- Abatacept: ?signal in IIM
- Tociluzimab:?IL-6 as a risk of ILD progression
- Emerging antifibrotic therapy trials in CTD/ILD
- **Lung transplant evaluation often concomitant with treatment**
- Oxygen, immunizations and pneumocystis prophylaxis

# Clinical trials in CTD ILD: Just starting!

- Scleroderma: SLS I , SLS II ( MMF vs CYC)
- Scleroderma: Tociluzimab in SSc
- Scleroderma: Rituxan
- Scleroderma: bone marrow transplantation
- RA: Open label Rituxan
- Upcoming FDA approved therapies in IPF i.e. clinical trials in scleroderma and RA
- IIM ?signal abatacept in ILD/IIM

# Ongoing IPF Trials

| | | 1 | 2 | 3 |
|---|---|---|---|---|
| Co-trimoxazole | | | | X |
| N-acetylcysteine | PANTHER-IPF | | | X |
| CNTO 888 | | X | | |
| IW001 | | X | | |
| Lebrikizumab | | | X | |
| CC-930 | | | X | |
| GS-6624 - Simtuzumab | | | X | |
| Tralokinumab | | | X | |
| FG-3019 | | | X | |
| GC1008 | | X | | |
| CT-2009 STX-100 | | | X | |
| Inhaled Nitric Oxide | | | X | |
| Inhaled C- Monoxide | | | X | |
| PRM-151 | | X | | |

# OMERACT in CTD/ILD (Current Respir Med Rev 2015)J Rheum 2014 )

- Physiologic (% predicted decline FVC)
- HRCT scoring systems (maximum fibrosis scores in zone of max disease, TLI and computer aided quantification)
- Cough
- Dyspnea scales
- HRQoL
- What about composite indices and will they vary in different CTD?

## OMERACT in CTD/ILD

- These agreed upon domains need to be validated in large cohorts/studies
- Outcome measures may be different for different CTD ILD

## Board Question 1

- Which antibody portends the highest risk for ILD?
- A. Rheumatoid factor
- B. ANCA
- C ANA
- D MDA-5 ab

## Answer to Question 1

- D MDA 5 ab
- This antibody is associated with amyopathic dermatomyositis, and has a high rate of ILD often severe and progressive

## Question II

- Which risk factors in RA portend increased risk for the development of ILD?
- A high titer RF
- B Smoking History
- CMale gender
- D Older age
- E All of the above

## Answer is E

- All of the above have been associated with a greater risk for the development of ILD in pts with RA

## Work together!

## Financial disclosures

- Up to Date
- Boerhringer Ingleheim